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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/723,197	11/27/2000	Kathleen E. Rodgers	97,017-P7	4161

20306 7590 07/02/2003

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EXAMINER
KAM, CHIH MIN

ART UNIT	PAPER NUMBER
1653	15

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/723,197	RODGERS ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-10,14 and 19-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-10,14,19-28 and 30-47* is/are rejected.

7)☒ Claim(s) *29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. The finality of the previous Office Action (Paper No. 10) is withdrawn because a new ground of rejection is applied in this Office Action.

Status of the Claims

2. Claims 1, 7-10, 14 and 19-47 are pending.

Applicant's amendment and terminal disclaimer filed on June 4, 2003 (Paper Nos. 13 and 14) are acknowledged. Applicants' response has been fully considered. Claim 1 has been amended. Thus, claims 1, 7-10, 14 and 19-47, and SEQ ID NO:4 are examined.

Objection Withdrawn

3. The previous objection to claims 1, 7-10, 19-28 and 30-47 regarding recitation of non-elected sequences in the claim, is withdrawn in view of applicants' amendment to the claim and applicants' response at page 6 in Paper No. 13.

Rejection Withdrawn

Claim Rejections-Obviousness Type Double Patenting

4. The previous rejection of claims 1, 7-10, 14 and 19-29 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of Patent 6,475,988, is withdrawn in view of applicants' submission of the terminal disclaimer in Paper No. 14, and applicants' response at page 6 in Paper No. 13.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 7-10, 14, 19-28 and 30-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an improved method of treating certain chemotherapy side effects such as hematopoietic toxicity, decreased mobilization of hematopoietic progenitor cells from bone marrow into the peripheral blood, and myelosuppression, wherein the improvement comprises administering to a human chemotherapy patient an effective amount of an active agent comprising a specific fragment of Angiotensin II (AII), e.g., AII(1-7) (SEQ ID NO:4), AII(1-6) or AII(1-5); a pharmaceutical composition comprising the active agent and optionally a cytokine; or an article of manufacture comprising the pharmaceutical composition, does not reasonably provide enablement for an improved method for treating or preventing (not even occur the first time) a chemotherapy side effect, wherein the improvement comprises administering to a human patient an effective amount of an active agent comprising a sequence consisting of at least three, four, five, six or seven contiguous amino acids in the sequence of formula I (R^1-R^2-R^3-R^4-R^5-R^6-R^7-R^8), wherein the side effect of chemotherapy is not defined; a pharmaceutical composition comprising the active agent and optionally a cytokine; or an article of manufacture comprising the pharmaceutical composition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1, 7-10, 14, 19-28 and 30-47 encompass an improved method for chemotherapy in a human patient, the improvement comprises administering an effective amount of an active agent comprising a sequence consisting of at least three contiguous amino acids in the sequence

of formula I (R^1-R^2-R^3-R^4-R^5-R^6-R^7-R^8) (claims 1, 7-10, 14, 19-27 and 35-47), a pharmaceutical composition comprising the active agent and optionally a cytokine (claims 28-32); or an article of manufacture comprising the pharmaceutical composition (claims 33 and 34). The specification, however, only discloses cursory conclusions (page 3, line 20-page 4, line 3) without data supporting the findings, which state that the invention provides a method for increasing hematopoietic cell survival following chemotherapy, for reducing or preventing other side effects of chemotherapy such as anemia, and for mobilizing hematopoietic progenitor cells from bone marrow into peripheral blood, comprising administering an effective amount of angiotensin II, or analogs or fragments thereof. There are no indicia that the present application enables the full scope in view of the process of the prevention or treatment of chemotherapy side effects using AII fragments as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the claims are enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding AII fragments and the effects of these fragments in the treatment and prevention of chemotherapy side effects, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

Examples 2-4 indicates the effect of AII(1-7), AII(1-6) or AII(1-5) on white blood cell mobilization and recovery after 5-fluorouracil treatment, and on hematopoietic recovery after cytoxan treatment in mice model, and Example 5 indicates the effect of AII(1-7) in chemotherapy patient, however, there are no working examples indicating the prevention of chemotherapy side effects using an AII fragment, nor demonstrating the effect of any shorter AII fragment.

(3). The state of the prior art and relative skill of those in the art:

Angiotensin II (AII) and its sarcosine analogs have been used in combination with cytotoxic drugs to induce hypertension in humans and experimental animals undergoing intra-arterial and intraperitoneal chemotherapy, and the use of AII is intended to increase blood flow to the tumor vasculature, thereby increasing the delivery of cytotoxic agent to the tumor (page 10, lines 16-23 of the specification). However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on how to prevent chemotherapy side effects by administering AII fragments and the effects of these fragments in the treatment of various chemotherapy side effects to be considered enabling.

(4). Predictability or unpredictability of the art:

The claims encompass treating or preventing chemotherapy side effects using various AII fragments, however, the conditions for preventing chemotherapy side effects, and the effects of shorter AII fragments are not described in the specification, the invention is highly unpredictable regarding the outcome of the treatment.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to an improved method for chemotherapy in a human patient, the improvement comprises administering an effective amount of an active agent comprising a sequence consisting of at least three contiguous amino acids in the sequence of formula I (R^1-R^2-R^3-R^4-R^5-R^6-R^7-R^8), a pharmaceutical composition comprising the active agent and optionally a cytokine; or an article of manufacture comprising the pharmaceutical composition. The specification indicates AII(1-7), AII(1-6) or AII(1-5) can increase hematopoietic cell survival following chemotherapy, and mobilize hematopoietic progenitor cells from bone marrow into peripheral blood in animal models and human patient (Examples 2-5). However, the specification has not demonstrated the administration of an AII fragment can actually prevent various chemotherapy side effects, nor has indicated how the effects of the AII fragment on chemotherapy side effects being monitored if the symptoms were prevented to occur. Furthermore, there is no example indicating an AII fragment with three or four contiguous amino acids is effective in treating various chemotherapy side effects. Since the specification fails to provide sufficient teachings on how to prevent chemotherapy side effects using various AII fragments (at least three contiguous amino acids of formula I), and the effect of AII fragments in the treatment various chemotherapy side effects, it is necessary to carry out further experimentation to assess the effects of various AII fragments in treating chemotherapy side effects.

(6). Nature of the Invention

The scope of the claims includes treating or preventing chemotherapy side effects using AII fragments, but the specification has not demonstrated how various chemotherapy side effects are being prevented using AII fragments, and what effects the shorter AII fragments have in the treatment. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed method, the outcome of claimed method is unpredictable, and the teaching in the specification is limited, therefore, it is necessary to have additional guidance on the treatment and prevention chemotherapy side effects using the AII fragments.

7. Claim 29 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

8. Claims 1, 7-10, 14, 19-28 and 30-47 are rejected, and claim 29 is objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner
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June 30, 2003

Christopher S. F. Low

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